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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,467	09/10/2003	Michael J. Welsh	P05405US01	6078

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DES MOINES, IA 50309-2721

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/659,467	WELSH ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *5-23 and 26-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,24,25,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 10 September 2003, has been entered into the record. Applicant's election of Invention I (Claims 1-11, 24-26, 30 and 31), and the species *Post-Traumatic Stress Disorder* in the paper of 30 October 2007, is acknowledged. The election was made without traverse.

Claims 5-23 and 26-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Inventions, there being no allowable generic or linking claims.

Claims 1-4, 24, 25, 30 and 31 are under examination in the Instant Application.

Claim Rejections/Objections

Claim Rejections - 35 USC § 112, second paragraph, indefiniteness.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.**

Claim 30 is rejected under 35 U.S.C. 112, -second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites a "CNS disorder characterized by extracellular pH." However, one skilled in the art cannot determine what is meant by the phrase. Perhaps applicants meant to

refer to "a change" in pH, since it is known that such a change has an effect on the ASIC receptor.

Appropriate Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph - Lack of Enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-4, 24, 25, 30 and 31 are rejected under 35 USC 112, first paragraph, because the specification does not enable a method of treating anxiety or an anxiety disorder, including *Post-Traumatic Stress Disorder* (PTSD) by administering an ASIC antagonist. The claims recite a method of treating an anxiety disorder in a patient, implying that such a disease is related to the ASIC receptor, without data or references identifying the disease as related to the ASIC receptor. Furthermore, the claimed treatments do not flow obviously from the instant disclosure, since no connection was made between the ASIC receptor and underlying mechanisms of anxiety disorders, such as PTSD.

Claims 1-4, 24, 25, 30 and 31 are directed to methods of treating an anxiety disorder by administering an antagonist of the ASIC receptor. Dependent claims further recite antagonists specific for the ASIC1 receptor, routes of administration of the antagonist, pharmaceutical compositions comprising the ASIC antagonist, as well as specific anxiety disorders. However,

according to the instant Disclosure, no pharmaceutically-acceptable compositions were produced, nor was an ASIC receptor antagonist administered to animals or humans.

The Specification as filed describes several experiments that confirm the role of the ASIC receptor in some neural activity in the hippocampus and amygdala. Data are presented showing the presence of the ASIC receptor in several brain regions involved in short-term memory and in conditioned fear responses. ASIC receptor knockout mice were produced that had mild deficits in tests of conditioned fear responses. The deficits were considered mild based on the fact that they could be overcome with increased training or stronger stimuli (page 34, Specification). Applicants demonstrated deficits in the animals in terms of some cranial nerve reflexes, some conditioned responses, and spatial memory, which is in keeping with the demonstrated locations of ASIC receptors in hippocampus, brainstem and amygdala (Wemmie, et al, 2002, Neuron, 34: 463-477, of record). Likewise, disclosed experiments showed that lower pH appears to be a stimulus for the ASIC receptor, but the data did not disclose or suggest a peptide or small molecule that could be administered as an ASIC ligand to an animal or human subject.

The instant Application does not reasonably provide enablement for a method of treating an anxiety disorder using an antagonist of the ASIC receptor without confirming that the diseases embraced by the claims involve the ASIC receptor. No data are presented in the Specification in which a naturally-occurring ASIC receptor-related disease is studied. In the case of claims encompassing medical treatments, additional enabling experiments are needed to confirm that ASIC receptor antagonists can be administered to treat anxiety disorders, such as PTSD. This is critically important since it is not known if anxiety disorders are caused or made worse by the ASIC receptor. Furthermore, anxiety disorders, especially PTSD, are difficult to treat

successfully, even if there are suggestions from the literature about the parts of the brain involved in fear responses (Rogan, et al, 1997, Nature, 390: 604-607, of record). Furthermore, the specification gives examples in which ASIC knockout mice had deficits in learning fear conditioning. However, none of the experiments prevented or treated a disease *in vivo*. And no nexus was made between the weak conditioned response of the animals and PTSD.

Although experimentation is not required for a method of treatment, the art does not disclose a nexus between the ASIC receptor and mechanisms underlying an anxiety disorder. In addition, the instant Disclosure does not discuss a nexus between ASIC antagonists and anxiety disorders.

Due to the large quantity of experimentation necessary to identify and treat anxiety disorders in an animal or human patient using an ASIC receptor antagonist, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims--undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, first paragraph - Written Description.

Claims 1-3 and 24 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention.

Claims 1-3 and 24 are directed to methods of treating an anxiety disorder using an ASIC antagonist. Dependent claims recite pharmaceutical compositions comprising the ASIC receptor antagonist, as well as several routes of administration of the composition. However, the specification does not teach any ASIC antagonists, nor are ASIC antagonists known in the literature.

To provide evidence of enablement of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a recitation of methods that use an ASIC antagonist. There is not even identification of any probable chemical compounds that bind ASIC. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of methods to use the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the methods of use of the antagonist referred to above, the skilled artisan cannot envision the detailed chemical compounds that could be used as an ASIC antagonist. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The product *itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods of antagonizing ASIC using a known antagonist, but not the full breadth of the claims, meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion: Claims 1-4, 24, 25, 30 and 31 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW
14 January 2008

/Manjunath N. Rao, /
Supervisory Patent Examiner, Art Unit 1647